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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/992,221	11/06/2001	Tomohiro Tsuji	3029-75	7242

7590 11/27/2002
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EXAMINER

WEBER, JON P

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 11/27/2002

4

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

09/992,221

Applicant(s)

TSUJI ET AL.

Examiner

Jon P Weber, Ph.D.

Art Unit

1651

-- The MAILING DATE f this communicati n appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-8 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: .

Art Unit: 1651

Status of the Claims

Claims 1-8 have been presented for examination.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

Claims 1-8 are objected to because of the following informalities:

Step 1 of claim 1 would be more clear if the two substeps, lysing and staining, had subletters a) and b).

Step 3 of claim 1 is confusing because it has awkward syntax. There should be a comma after "erythroid cells".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Art Unit: 1651

Steps 4 and 5 of claim 1 are confusing and lack clear antecedent basis in that these steps are calculations and themselves do not constitute either classifying or counting nucleated bone marrow cells.

Step 7 of claim 2 is confusing and lacks clear antecedent basis in that the step is calculations and does not constitute either classifying or counting nucleated bone marrow cells.

Claim 3 is confusing and lacks clear antecedent basis in that the steps are calculations and does not constitute either classifying or counting nucleated bone marrow cells.

Other claims depend from a rejected claim and are rejected as well for the same reasons.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inami et al. (US 5,298,426) in view of Kim et al. (US 5,559,037), Hansen et al. (US 4,284,412) and Hoffman et al. (US 4,492,752) and further in view of Kim et al. (US 5,516,695).

Inami et al. (US 5,298,426) disclose a method of measuring the number of erythrocytic nucleated cells by the following steps: 1) a sample of blood cells containing erythroblasts is mixed with a hypotonic lysis solution at a pH of 3.5 to 5.0 to lyse the erythrocytes and further comprising a fluorescent nuclear dye to stain the nucleated cells differentially, and 2) then analyzed by flow cytometric analysis via scattered light and fluorescence. The different

Art Unit: 1651

nucleated cell types can be distinguished and counted (column 1, line 67 to column 2, line 24). Erythroblasts are normally found in the bone marrow and not in circulating blood, and their differentiation and counting is clinically important in the treatment of certain diseases such as anemia and leukemia (column 1, lines 25-31). Inami et al. (US 5,298,426) lack calculating ratios of the different cell types and the surfactant in the lysis solution.

Kim et al. (US 5,559,037) disclose taking a sample of blood cells, exposing it to a erythrocyte lysis solution further comprising a nuclear staining dye and analyzing the solution by flow cytometry using scattered light and fluorescence to distinguish and count the different nucleated cell types. A wide range of fluorescent dyes may be used (column 6, lines 18-56).

Hansen et al. (US 4,284,412) disclose taking a sample of blood cells, incubating them with a fluorescent antibody specific to a subclass of cell antigens, lysing the erythrocytes in the sample in the conventional fashion, and analyzing the resulting sample by flow cytometry by means of scattered light and fluorescence (column 5, lines 40 to column 6, line 34) so as to count the identified cells.

Hoffman et al. (US 4,492,752) provides a similar disclosure to Hansen et al. (US 4,284,412) but wide-angle scattering is used.

Kim et al. (US 5,516,695) disclose a multipurpose reagent system for the rapid lysis of erythrocytes in blood samples to be analyzed by flow cytometry via scattered light and fluorescence. The multipurpose reagent comprises: quaternary ammonium salts (column 6, lines 50-58), aliphatic aldehyde (column 6, line 59 to column 7, line 3), non-phosphate buffer (column 7, lines 4-20) surface active agents such as saponin (column 7, line 21-58), anticoagulant, nuclear stain or antibody with an osmolarity is between about 160 and 310 mOsm/L (column 5, lines 30-

Art Unit: 1651

45). The reagent is said to completely lyse the erythrocytes while maintaining the white blood cells.

A person of ordinary skill in the art at the time the invention was made would have been motivated to use the method of Inami et al. (US 5,298,426) using the lysis buffer like that of Kim et al. (US 5,516,695) because the lysis buffer of Kim et al. (US 5,516,695) is said to completely lyse the erythrocytes while being gentle enough on the other cells in the blood sample, even the fragile ones, to maintain their integrity. Kim et al. (US 5,559,037), Hansen et al. (US 4,284,412), Hoffman et al. (US 4,492,752) and Kim et al. (US 5,516,695) all show that using a combination of scattered light and fluorescence in a flow cytometry method to measure and count nucleated cells is well known in the art. The further analysis of the data involving calculations of ratios of measured counts involves nothing more than mental steps and is not accorded patentable weight. That is, no further physical steps are involved just already measured parameters are compared. These additional steps constitute an algorithm. Inami et al. (US 5,298,426) do not exemplify taking bone marrow directly, but blood that contains erythroblasts. Inami et al. (US 5,298,426) explicitly suggest that the erythroblasts are found primarily in bone marrow. Hence there is a reasonable suggestion to analyze the erythrocytic cells in bone marrow.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use the lysis buffer of Kim et al. (US 5,516,695) in the method of Inami et al. (US 5,298,426) to analyze the nucleated cells from bone marrow with flow cytometry via scattered light and fluorescence. Kim et al. (US 5,559,037), Hansen et al. (US 4,284,412), Hoffman et al. (US 4,492,752) and Kim et al. (US 5,516,695) establish that the

Art Unit: 1651

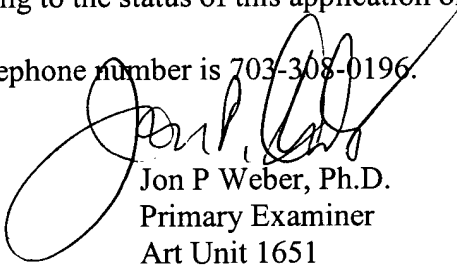
general method of analyzing the nucleated cells in a blood sample in this manner was well known in the art.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jon P Weber, Ph.D.
Primary Examiner
Art Unit 1651

JPW
November 26, 2002